

Claims

1. A method for inhibiting cytoskeletal rearrangement in a cell or cell fragment, comprising:

5 contacting the cell or cell fragment with an amount of a Fyb/SLAP complex inhibitor sufficient to inhibit the formation of a complex of an Ena/VASP protein and a Fyb/SLAP protein.

10 2. The method of claim 1, wherein the Fyb/SLAP complex inhibitor binds to the EVH1 domain of the Ena/VASP protein and inhibits binding of the Ena/VASP protein to a Fyb/SLAP protein.

15 3. The method of claim 2, wherein the Ena/VASP family protein is selected from the group consisting of Ena, Mena, VASP and Ev1.

20 4. The method of claim 2, wherein the Fyb/SLAP complex inhibitor comprises the peptide FPPPP (SEQ ID NO:15) or a peptide mimetic having an equivalent binding specificity.

25 5. The method of claim 4, wherein the Fyb/SLAP complex inhibitor is selected from the group consisting of ActA repeats, EVH1 binding peptides, ScarWA, and dominant negative Fyb/SLAP fragments.

30 6. The method of claim 1, wherein the Fyb/SLAP complex inhibitor binds a Fyb/SLAP protein and inhibits binding of an Ena/VASP protein to the Fyb/SLAP protein.

25 7. The method of claim 6, wherein the Fyb/SLAP complex inhibitor is a polypeptide which has a functional EVH1 domain but which cannot function as an Ena/VASP protein in cytoskeletal rearrangement of the cell or cell fragment.

30 8. The method of claim 6, wherein the Fyb/SLAP complex inhibitor is an antibody or antibody fragment which binds Fyb/SLAP.

9. The method of claim 1, wherein the Fyb/SLAP complex inhibitor is an antisense nucleic acid molecule which inhibits the expression of a Fyb/SLAP protein or an Ena/VASP protein.

5 10. The method of claim 1, wherein the Fyb/SLAP complex inhibitor is administered *in vivo* to a subject in need of such treatment.

11. The method of claim 1, wherein the cell is a lymphocyte or a macrophage.

10 12. The method of claim 11, wherein the lymphocyte is a T cell.

13. The method of claim 1, wherein the cell fragment is a platelet.

14. A method for inhibiting cytoskeletal rearrangement in a cell or cell fragment,
15 comprising:
 inhibiting the expression of a Fyb/SLAP protein sufficiently to inhibit the formation of a complex of an Ena/VASP protein and a Fyb/SLAP protein.

15. A method for enhancing cytoskeletal rearrangement in a cell or cell fragment,
20 comprising:
 contacting the cell or cell fragment with an amount of a composition which increases the amount of a Fyb/SLAP polypeptide in the cell or cell fragment sufficient to enhance the formation of a complex of an Ena/VASP protein and a Fyb/SLAP protein

25 16. The method of claim 15, wherein the composition is a Fyb/SLAP polypeptide.

17. The method of claim 15, wherein the composition is a nucleic acid molecule which encodes a Fyb/SLAP polypeptide.

30 18. The method of claim 15, wherein the composition which increases the amount of a Fyb/SLAP polypeptide is administered to a subject in need of such treatment *in vivo*.

19. The method of claim 15, wherein the cell is a lymphocyte or a macrophage.

20. The method of claim 19, wherein the lymphocyte is a T cell.

21. The method of claim 15, wherein the cell fragment is a platelet.

5 22. A method for increasing a T cell response to T cell receptor stimulation, comprising: contacting a T cell with a Fyb/SLAP complex activator sufficient to promote the formation of a complex of an Ena/VASP protein and a Fyb/SLAP protein in the T cell.

10 23. The method of claim 22, wherein the Fyb/SLAP activator is administered *in vivo* to a subject in need of such treatment.

24. The method of claim 23, wherein the subject has or is at risk of developing an infectious disease.

15 25. The method of claim 23, wherein the subject has or is at risk of developing cancer.

26. A method for inhibiting a T cell response to T cell receptor stimulation, comprising: contacting a T cell with an amount of a Fyb/SLAP complex inhibitor sufficient to inhibit formation of a complex of a Fyb/SLAP protein and an Ena/VASP protein in the T cell.

20 27. The method of claim 26, wherein the Fyb/SLAP inhibitor is administered *in vivo* to a subject in need of such treatment.

25 28. The method of claim 27, wherein the subject has or is at risk of developing an autoimmune disease.

29. The method of claim 27, wherein the subject has or is at risk of developing a condition characterized by inflammation.

30 30. The method of claim 26, wherein the Fyb/SLAP complex inhibitor binds to the EVH1 domain of the Ena/VASP protein and inhibits binding of the Ena/VASP protein to a Fyb/SLAP protein.

31. The method of claim 30, wherein the Ena/VASP family protein is selected from the group consisting of Ena, Mena, VASP and Ev1.

5 32. The method of claim 30, wherein the Fyb/SLAP complex inhibitor comprises the peptide FPPPP (SEQ ID NO:15) or a peptide mimetic having an equivalent binding specificity.

10 33. The method of claim 32, wherein the Fyb/SLAP complex inhibitor is selected from the group consisting of ActA repeats, EVH1 binding peptides, ScarWA, and dominant negative Fyb/SLAP fragments.

15 34. The method of claim 26, wherein the Fyb/SLAP complex inhibitor binds a Fyb/SLAP protein and inhibits binding of an Ena/VASP protein to the Fyb/SLAP protein.

20 35. The method of claim 34, wherein the Fyb/SLAP complex inhibitor is a polypeptide which has a functional EVH1 domain but which cannot function as an Ena/VASP protein in cytoskeletal rearrangement of the cell or cell fragment.

25 36. The method of claim 34, wherein the Fyb/SLAP complex inhibitor is an antibody or antibody fragment which binds Fyb/SLAP.

37. The method of claim 26, wherein the Fyb/SLAP complex inhibitor is an antisense nucleic acid molecule which inhibits the expression of a Fyb/SLAP protein or an Ena/VASP protein.

25 38. The method of claim 26, wherein the Fyb/SLAP complex inhibitor is administered *in vivo* to a subject in need of such treatment.

30 39. A method for increasing platelet aggregation, comprising:
contacting a platelet with Fyb/SLAP complex inhibitor to inhibit formation of a complex of a Fyb/SLAP protein and an Ena/VASP protein in the platelet.

40. The method of claim 39, wherein the Fyb/SLAP inhibitor is administered *in vivo* to a subject in need of such treatment.

41. The method of claim 40, wherein the administration of the Fyb/SLAP inhibitor
5 increases wound healing or clotting.

42. The method of claim 39, wherein the Fyb/SLAP complex inhibitor binds to the EVH1 domain of the Ena/VASP protein and inhibits binding of the Ena/VASP protein to a Fyb/SLAP protein.

10 43. The method of claim 42, wherein the Ena/VASP family protein is selected from the group consisting of Ena, Mena, VASP and Ev1.

15 44. The method of claim 42, wherein the Fyb/SLAP complex inhibitor comprises the peptide FPPPP (SEQ ID NO:15) or a peptide mimetic having an equivalent binding specificity.

20 45. The method of claim 44, wherein the Fyb/SLAP complex inhibitor is selected from the group consisting of ActA repeats, EVH1 binding peptides, ScarWA, and dominant negative Fyb/SLAP fragments.

46. The method of claim 39, wherein the Fyb/SLAP complex inhibitor binds a Fyb/SLAP protein and inhibits binding of an Ena/VASP protein to the Fyb/SLAP protein.

25 47. The method of claim 46, wherein the Fyb/SLAP complex inhibitor is a polypeptide which has a functional EVH1 domain but which cannot function as an Ena/VASP protein in cytoskeletal rearrangement of the cell or cell fragment.

30 48. The method of claim 46, wherein the Fyb/SLAP complex inhibitor is an antibody or antibody fragment which binds Fyb/SLAP.

49. The method of claim 39, wherein the Fyb/SLAP complex inhibitor is an antisense nucleic acid molecule which inhibits the expression of a Fyb/SLAP protein or an Ena/VASP protein.

5 50. The method of claim 39, wherein the Fyb/SLAP complex inhibitor is administered *in vivo* to a subject in need of such treatment.

51. A composition comprising an effective amount of a Fyb/SLAP complex inhibitor and a pharmaceutically acceptable carrier.

10 52. The composition of claim 51, wherein the Fyb/SLAP complex inhibitor comprises the peptide FPPPP (SEQ ID NO:15) or a peptide mimetic having an equivalent binding specificity.

15 53. The composition of claim 52, wherein the Fyb/SLAP complex inhibitor is selected from the group consisting of ActA repeats, EVH1 binding peptides, ScarWA, and dominant negative Fyb/SLAP fragments.

54. The composition of claim 51, wherein the Fyb/SLAP complex inhibitor binds a 20 Fyb/SLAP protein and inhibits binding of an Ena/VASP protein to the Fyb/SLAP protein.

55. The composition of claim 54, wherein the Fyb/SLAP complex inhibitor is a polypeptide which has a functional EVH1 domain but which cannot function as an Ena/VASP protein in cytoskeletal rearrangement of the cell or cell fragment.

25 56. The composition of claim 54, wherein the Fyb/SLAP complex inhibitor is an antibody or antibody fragment which binds Fyb/SLAP.

57. The composition of claim 51, wherein the Fyb/SLAP complex inhibitor is an antisense 30 nucleic acid molecule which inhibits the expression of a Fyb/SLAP protein or an Ena/VASP protein.

58. A composition comprising an effective amount of a Fyb/SLAP complex activator and a pharmaceutically acceptable carrier.

59. The composition of claim 58, wherein the Fyb/SLAP complex activator is a
Fyb/SLAP polypeptide or a nucleic acid molecule which encodes a Fyb/SLAP polypeptide.

60. An isolated antibody which selectively binds human Fyb/SLAP 2 but not Fyb/SLAP1.

61. The isolated antibody of claim 60, wherein the antibody binds to SEQ ID NO:7.
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62. The isolated antibody of claim 60, wherein the antibody binds to an epitope defined by amino acids 637-682 of SEQ ID NO:4.

63. An isolated antibody which selectively binds Arp3 polypeptide, wherein the antibody binds to an epitope formed by the amino acids set forth in SEQ ID NO:11.
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64. An isolated human Fyb/SLAP2 polypeptide comprising the amino acids 637-682 of SEQ ID NO:4.

20 65. The isolated human Fyb/SLAP2 polypeptide of claim 64, wherein the amino acid sequence comprises SEQ ID NO:4

66. An isolated nucleic acid molecule which encodes the human Fyb/SLAP2 polypeptide of claim 64.
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67. The isolated nucleic acid molecule of claim 66, wherein the nucleic acid molecule comprises nucleotides 1939-2076 of SEQ ID NO:5.

68. The isolated nucleic acid molecule of claim 66, wherein the nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:5.
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69. An expression vector comprising the isolated nucleic acid molecule of any of claims 66-68 operably linked to a promoter.

70. A host cell transformed or transfected with the expression vector of claim 69.

71. A method for identifying lead compounds for a pharmacological agent useful in the treatment of disease associated with Fyb/SLAP-Ena/VASP complex formation, comprising
5 forming a mixture comprising a Fyb/SLAP protein or EVH1 domain binding fragment thereof, a Ena/VASP protein or Fyb/SLAP binding fragment thereof, and a candidate pharmacological agent,
incubating the mixture under conditions which, in the absence of the candidate
10 pharmacological agent, permit a first amount of specific binding of the Fyb/SLAP protein or EVH1 domain binding fragment thereof and the Ena/VASP protein or Fyb/SLAP binding fragment thereof, and
detecting a test amount of the specific binding of the Fyb/SLAP protein or EVH1 domain binding fragment thereof and the Ena/VASP protein or Fyb/SLAP binding fragment thereof, wherein an increase in the test amount of specific binding in the presence of the candidate pharmacological agent relative to the first amount of specific binding indicates that the candidate pharmacological agent is a lead compound for a pharmacological agent which increases specific binding of the Fyb/SLAP protein or EVH1 domain binding fragment thereof and the Ena/VASP protein or Fyb/SLAP binding fragment thereof, and wherein a
15 decrease in the test amount of specific binding in the presence of the candidate pharmacological agent relative to the first amount of specific binding indicates that the candidate pharmacological agent is a lead compound for a pharmacological agent which decreases specific binding of the Fyb/SLAP protein or EVH1 domain binding fragment thereof and the Ena/VASP protein or Fyb/SLAP binding fragment thereof.
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72. A method for identifying lead compounds for a pharmacological agent useful in the treatment of disease associated with Fyb/SLAP-Ena/VASP complex formation, comprising
contacting a Fyb/SLAP protein or EVH1 domain binding fragment thereof with a candidate pharmacological agent, and
determining the binding of the candidate pharmacological agent to the Fyb/SLAP protein or EVH1 domain binding fragment thereof.
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